HIV in Adolescents and Young Adults

Introduction

Background

Adolescence and young adulthood is a period of intense physical and developmental transition that is characterized by experimentation and self-discovery.[1] This time period may pose unique challenges for the prevention and treatment of HIV.[2] Adolescents and young adults living with HIV in the United States primarily represent two distinct groups based on when and how they acquired HIV: (1) those who acquired HIV through perinatal transmission and now have reached the age of adolescence or young adulthood, and (2) those who acquired HIV during adolescence or young adulthood through sexual contact or drug use.[3,4] In addition, rare cases of HIV acquisition occur in childhood as a result of child sexual abuse.[5,6] In the United States, since the contemporary perinatal HIV transmission rate has been reduced to less than 1% of pregnancies in women living with HIV, most adolescents and young adults living with HIV have acquired HIV via sexual activity.[2]

HIV Care Cascade/HIV Continuum of Care

Limited data exist regarding the HIV Care Cascade or HIV Continuum of Care in adolescents and young adults in the United States.[7,8] A 2010 estimate of the HIV Care Cascade for persons aged 13-29 years showed a marked drop-off at every point in the continuum; in this model, only 40% of the estimated numbers of youth living with HIV were diagnosed, 25% linked to care, 11% retained in care, and only 6% had obtained virologic suppression (Figure 1).[7] In later data extrapolated from 2014 CDC surveillance data of persons living with HIV aged 13-24 years, the overall rates of virologic suppression were 25%, but again, there were major drop-offs from those living with HIV to those diagnosed, linked, and retained in care (Figure 2).[8]

Definition of Adolescents and Young Adults

In the Centers for Disease Control and Prevention (CDC) surveillance reports, adolescents are defined as persons 13 to 19 years of age and young adults are defined as persons 20 to 24 years of age, unless otherwise specified.[4] The Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV defines adolescents as postpubertal adolescents who have a sexual maturity rating of IV or V (Table 1).[2,9]

Health Care for Adolescents and Young Adults with HIV

Despite steps in the right direction, there is a relative lack of data on the needs of adolescents and young adults who are living with HIV, and more research is needed to develop optimal strategies for diagnosing and managing youth with HIV.[10,11] Optimal care should include a medical provider with adolescent expertise and a clinic environment that incorporates a youth medical home model with a focus on family-centered care while maintaining patient trust and confidentiality (Figure 3).[12]
This Topic Review will address routine care for adolescents and young adults living with HIV, adolescent sexuality and reproductive health, transitioning from adolescent to adult care, and preexposure prophylaxis in adolescents and young adults at risk for HIV infection.
Epidemiology of HIV in Adolescents and Young Adults

2014 HIV Surveillance Case Definition

The CDC established the first HIV surveillance case definition in 1982, with major revisions released in 1987, 1993, 2008, and most recently in 2014. The 2014 case definition establishes criteria for confirming a diagnosis of HIV infection, including laboratory and clinical evidence, as well as criteria for classifying the stage of HIV infection (stage 0, 1, 2, 3, or unknown).[14] Historically, children younger than age 13 were classified separately from adults and adolescents.[14] The 2014 case definition applied a single HIV case definition to persons of all ages. It also specified a different CD4 criteria for staging pediatric HIV infection among three age groups: less than 1 year, ages 1 to 5 years, and age 6 years and older. The 2014 case definition did not change the staging criteria for adolescents or adults. The following summarizes recent HIV surveillance data in adolescents and young adults.

Adolescents and Young Adults with Diagnosed HIV

At year-end 2015, 36,478 adolescents and young adults were living with diagnosed HIV in the United States.[15] Adolescents and young adults together comprised approximately 4% of the total number of persons living with diagnosed HIV infection in the United States at year-end 2015 (Figure 4), but accounted for 21.2% of persons newly-diagnosed with HIV in 2015 (Figure 5).[8] In 2015, the rate per 100,000 population of new diagnoses was 8.0 for adolescents aged 15 to 19 years and 31.2 for young adults 20 to 24 years of age.[16] For both adolescents and young adults, the number newly diagnosed with HIV remained relatively stable from 2011 to 2016 (Figure 6).[8]

Race/Ethnicity

In 2015, among the 36,478 adolescents and young adults living with diagnosed HIV in the United States, 21,551 (59%) were black/African American, 7,731 (22%) Hispanic/Latino, and 4,972 (14%) white (Figure 7).[8] In addition, the 2015 rates of diagnosed HIV in the United States, for age groups 13-14, 15-19, and 20-24 years were much greater in black/African Americans than any other racial/ethnic group (Figure 8).[8] In 2016, among the 8,451 new HIV diagnoses in adolescents and young adults, 4,628 (55%) were black/African-American, 1,960 (23%) were Hispanic/Latino, and 1,435 (17%) were white (Figure 9).[8]

Geographic Region

Among the 36,460 adolescents and young adults living with diagnosed HIV in 2015, 18,773 (51%) were living in the South, 7,165 (20%) in the Northeast, 5,400 (15%) in the Midwest, and 5,122 (15%) in the West (Figure 10).[17] Among the 8,540 adolescents and young adults newly diagnosed with HIV infection in 2016, 4,606 (54%) were living in the South, which was at least 3-fold greater than any other region.[17]

Transmission Categories

The following summarizes HIV transmission category data in the United States for adolescents and young adults, both for newly-diagnosed HIV infections in 2015 and for persons living with diagnosed HIV at year-end 2015.[15] These data indicate two different HIV populations in adolescents and young adults—those who were infected through perinatal transmission and those who acquired HIV behaviorally, typically through sex or injection drug use.[18] In 2015, for persons aged 13 to 24 years with newly diagnosed HIV, 88% were males.[15] For males aged 13 to 24 years with newly diagnosed HIV in 2015, 92% were attributed to male-to-male sexual contact.[4] For females aged 13 to 24 years with newly diagnosed HIV in 2015, 88% acquired HIV infection through heterosexual sex and 11% by injection drug use.[4] The age and transmission category for adolescents and young...
adults living with diagnosed HIV infection at year-end 2015 are listed below:[17]

- **HIV Infection by Sex:** For persons aged 13 to 24 years living with HIV at year-end 2015, 77% were males and 23% females.
- **Males Aged 13 to 19 Years:** For males living with HIV aged 13 to 19 years, 54% acquired HIV via male-to-male sex, 37% by perinatal transmission, 2% by heterosexual sex, 2% by injection drug use and male-to-male sex, less than 1% by injection drug use alone, and 5% by other routes.
- **Females Aged 13 to 19 Years:** For females aged 13 to 19 years, 68% acquired HIV through perinatal transmission, 22% by heterosexual sex, 2% by injection drug use, and 9% via other routes.
- **Males Aged 20 to 24 Years:** For this age group, 85% of those living with HIV acquired HIV through male-to-male sex, 7% through perinatal transmission, 3% by heterosexual sex, 4% by injection drug use and male-to-male sex, 1% by injection drug use alone, and less than 1% by other routes.
- **Females aged 20 to 24 Years:** For this age group living with diagnosed HIV, 58% acquired HIV through heterosexual sex, 32% from perinatal transmission, 7% by injection drug use, and 3% via other routes.
Testing, Linkage to, and Retention in Care

CDC HIV Testing Recommendations for Adolescents and Young Adults

Since 2006, the CDC has recommended opt-out HIV testing for all persons between the ages of 13 and 64, unless the local prevalence of undiagnosed HIV infection has been documented to be less than 0.1%.[19] Accordingly, routine HIV screening should include adolescents and young adults. Testing should be performed annually (or more frequently) for individuals at higher risk of HIV—defined by CDC as persons who use injection drugs and their sex partners, persons who exchange sex for money or drugs, sex partners of persons with HIV, and men who have sex with men, or heterosexual persons who themselves or whose sex partners have had more than one sex partner since their most recent HIV test.[19]

HIV Risk and HIV Testing Rates

In the United States, Youth Risk Behavior Surveillance System (YRBSS) data demonstrates that many high school-aged youth regularly engage in sexual activity that could place them at risk of acquiring HIV infection. Among high school students in 2013, 47% reported having sexual intercourse at least once, 34% were sexually active, 41% reported condomless sex at last intercourse, and 15% reported having had 4 or more lifetime sex partners.[20] In a separate report, 22% of high school students who had ever had sexual intercourse had ever been tested for HIV; this same report showed that only 33% of young adults (aged 18 to 24 years) had ever been tested for HIV.[21] Other behavioral surveillance studies have found low rates of HIV testing among sexually active high school students, with no improvement in testing rates from 2005 to 2013, even among those with multiple lifetime partners (Figure 11).[22] Based on estimates from CDC surveillance data, adolescents and young adults with HIV infection have the lowest awareness of HIV status of any age group—44.4% of them were unaware of their HIV status in 2014; by comparison, among all people living with HIV in 2014, an estimated 15% were unaware of their HIV status (Figure 12).[16]

Point-of-Care Rapid HIV Testing

A systematic review of 14 studies evaluating the use of rapid point-of-care HIV testing found conclusive evidence that adolescents and young adults accept and prefer point-of-care rapid HIV testing platforms compared with traditional laboratory testing.[23] Avoiding venipuncture and obtaining results faster were key reasons that rapid testing was preferred, and the review also found that adolescents and young adults were likely to accept rapid testing when offered rather than having to ask for the test. There are, however, several caveats with point-of-care testing. First, most point-of-care tests have lower sensitivity than currently used fourth-generation antigen-antibody tests, particularly with respect to diagnosing very early HIV infection. Second, any positive point-of-care test will require a blood draw for confirmatory HIV testing. Last, many office settings do not have trained staff to perform point-of-care testing and obtaining a blood draw for a laboratory-based test is usually much more efficient.

Barriers to HIV Testing in Adolescents and Young Adults

The reasons for the discordance between HIV risk behavior and HIV testing rates in youth are myriad and include lack of knowledge about HIV risk, lack of perceived risk, sense of invulnerability to disease, lack of access to (or awareness of) free and confidential HIV testing sites, stigma, and misconception that parental consent is required for HIV testing.[18,23,24] Additional HIV testing barriers that have been identified are lack of medical provider awareness that CDC HIV testing recommendations include testing of adolescents and young adults, lack of medical insurance, and overall limited engagement with health systems.[22] Educating pediatricians and primary care medical providers about HIV testing recommendations for adolescents and young adults has the potential to increase HIV testing, especially given that a private physician office or other clinic site is
still the most likely setting for adolescents and young adults to get HIV testing, with fewer than 5% undergoing HIV testing at a designated HIV testing site (Figure 13). In Connect to Testing and Prevention Services, a demonstration study conducted by the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN), investigators evaluated strategies for increasing HIV testing among sexual minority males aged 13 to 24 years. Based on their findings, they concluded that universal HIV screening of adolescents and young adults may play an important role in reducing stigma, but this approach may not adequately reach populations, such as youth of color, at high risk for acquiring HIV. Specifically they found a community-based, targeted HIV testing approach was more effective than routine screening for sexual minority males aged 13 to 24 years.

Factors Affecting Linkage and Engagement in Care

For persons diagnosed with HIV infection, linkage to and retention in HIV clinical care are associated with improved clinical outcomes, decreased mortality, and decreased HIV transmission to sex and injecting-drug partners. Although significant research has been conducted on interventions to improve linkage to care for persons newly diagnosed with HIV infection, few studies have included adolescents and young adults. Therefore, the individual and structural barriers for linkage and engagement in HIV care that are unique to adolescents and young adults remain poorly defined. Adolescents and young adults living with HIV may struggle to navigate complex medical systems, especially as they transition from pediatric to adult health centers; during this transition many adolescents and young adults lack full autonomy as they remain dependent on their families for health insurance, transportation, housing, and other needs. For those young adults who become infected with HIV while on a parental insurance plan, inadvertent disclosure of their HIV status may occur. Adolescents and young adults who are members of racial, ethnic, gender, or sexual minorities may face additional stigma. In addition, receiving an HIV diagnosis during the vulnerable period spanning adolescence and early adulthood can lead to higher rates of depression and anxiety that may serve as barriers to engagement in care.

Strategies for Improving Linkage and Retention in Care

Certain interventions are possible that can improve engagement along every step of the HIV care continuum. Adolescent-targeted (or adolescent-friendly) services include providing dedicated adolescent-only office hours, screening for sexually transmitted infections (of genital and extragenital sites), providing condoms and hormonal contraceptives, offering preexposure prophylaxis and nonoccupational postexposure prophylaxis, and linking to peer educators and adolescent support groups.
Clinical and Laboratory Monitoring

Baseline Evaluation for Newly Diagnosed Adolescent or Young Adult

For an adolescent or young adult newly diagnosed with HIV infection, the goals of the initial evaluation are the same as for adults and are outlined by the Department of Health and Human Services (HHS) guidelines: confirm the diagnosis of HIV infection, obtain a complete medical history, perform a physical examination, obtain relevant laboratory data, screen for sexually transmitted infections and substance use disorders, provide education about HIV, and link to appropriate primary care resources if necessary.[29] For younger adolescents, additional psychosocial intervention and additional education may be necessary, and this should ideally involve the parents or guardians, though this depends on multiple factors, including state law, institutional policy, maturity of the adolescent, and social situation. The initial evaluation of persons newly diagnosed with HIV is discussed in detail in the Initial Evaluation Topic Review in the Primary Care Module.

Routine Monitoring

Routine laboratory and clinical monitoring of adolescents and young adults living with HIV is the same as for older adults living with HIV and is outlined in the antiretroviral therapy guidelines.[30]
Choosing Antiretroviral Therapy Regimens

Initiating Antiretroviral Therapy for Adolescents and Young Adults

All adolescents and young adults with HIV infection should receive antiretroviral therapy, regardless of their CD4 cell count or HIV RNA level. [2] Teenagers or young adults who acquired HIV via perinatal transmission have typically been on antiretroviral therapy for many years prior to reaching adolescence; they often have complex antiretroviral regimens and higher pill burdens as a result of antiretroviral resistance mutations that accumulated over the many preceding years of receiving antiretroviral therapy. [31, 32, 33] All youth who become infected as a teenager or young adult should be started on antiretroviral therapy (if not already receiving). Prior to initiating antiretroviral therapy, careful attention should be given to the readiness of the adolescent or young adult to start antiretroviral therapy and their ability to adhere to therapy. [2] Prior to starting antiretroviral therapy in an adolescent or young adult, usual baseline testing, including an HIV drug resistance genotype should be ordered.

Choosing Antiretroviral Therapy Regimens

The selection and dosing of antiretroviral medications for adolescents is based on sexual maturity rating rather than on age. The recommended antiretroviral regimens for initial therapy for post-pubescent adolescents whose sexual maturity rating is IV or V, and for all young adults, are the same as for older adults with HIV (Table 2) and (Table 3). [34] For pre-pubescent adolescents with sexual maturity ratings between I and III, separate pediatric guidelines are available to guide the antiretroviral regimen selection and medication dosing. [35]

Laboratory Monitoring after Starting Antiretroviral Therapy

Routine laboratory and clinical monitoring of adolescents and young adults after starting antiretroviral therapy is the same as for older adults with HIV and is outlined below. [30, 36] The following summarizes recommendations in the Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV for monitoring HIV RNA levels and CD4 cell counts after starting antiretroviral therapy:

- **HIV RNA Monitoring:** All individuals initiating antiretroviral therapy should have a baseline HIV RNA level and a repeat level obtained 2-8 weeks after initiating therapy. Subsequently, HIV RNA levels should be repeated every 4-8 weeks until the viral load is suppressed. Once HIV RNA levels are suppressed, monitoring should be done every 3-4 months. For adherent patients who have consistently suppressed HIV RNA levels and stable immunologic status for at least 2 years, HIV RNA monitoring can be extended to 6-month intervals. If a patient has a change in clinical status or has to initiate therapy with chronic corticosteroids, chemotherapy, or interferon, the HIV RNA levels should be checked every 3 months.

- **CD4 Cell Count:** All persons starting on antiretroviral therapy should have a baseline CD4 cell count and a repeat value 3 months after starting therapy. During the first 2 years on antiretroviral therapy the CD4 count should be monitored every 3-6 months. After 2 years on antiretroviral therapy, for adherent patients who have consistently suppressed HIV RNA levels, the frequency of CD4 cell count monitoring can be based on CD4 cell count: (1) if the CD4 count is less than 300 cells/mm$^3$, monitoring should continue every 3-6 months, (2) if the CD4 count is consistently in the 300-500 cells/mm$^3$ range, monitoring can be extended to 12-month intervals, and (3) if the CD4 count is consistently greater than 500 cells/mm$^3$, monitoring may then be considered optional. If a patient has an increase in HIV RNA, a change in clinical status, or has to initiate therapy with chronic corticosteroids, chemotherapy, or interferon, the CD4 cell counts levels should be checked every 3-6 months.
Adherence to Antiretroviral Therapy

Challenges with Adherence to Antiretroviral Therapy

Poor adherence to antiretroviral therapy reduces the likelihood of virologic suppression, increases the risk of developing drug resistance mutations and virologic failure, limits future treatment options, and can lead to both disease progression and HIV transmission due to uncontrolled viremia. As a group, adolescents and young adults with HIV infection struggle with adherence more than their older adult counterparts and have lower rates of viral suppression and higher rates of viral rebound.[37] Cross-sectional observational studies have identified several barriers to antiretroviral medication adherence for adolescent populations, including poor understanding of the importance of adherence, denial and fear, chaotic lifestyles, forgetfulness, comorbid mental health diagnoses, substance use, lack of family and social support, fear of HIV disclosure to family members through insurance claims, and structural barriers such as homelessness.[2,38,39] In a study of adherence in youth (aged 12 to 24 years) with either perinatal HIV acquisition (“perinatal group”) or HIV acquisition through sexual activity or drug use (“behavioral group”), the two groups in the study had many overlapping adherence challenges, but also had distinct reasons for having problems with adherence [Table] Barriers to Medication Adherence, by Route of Infection Youth Aged 12 to 24.[38] Forgetting to take the medication was by far the most common adherence barrier in both groups.[38] Overall, the barriers were greater in the perinatal group and these youth often struggled with treatment fatigue and were more likely to report side effects from medications (likely due to higher pill burden and prior medication exposure).[38] In general, adolescents may be especially sensitive to side effects.[2]

Strategies for Improving Antiretroviral Adherence in Adolescents

The Pediatric Antiretroviral Therapy Guidelines outline recommendations for adherence monitoring (Table 5).[40] In addition, the Pediatric Antiretroviral Therapy Guidelines provide strategies for improving adherence that are focused on initial intervention strategies, medication strategies, and follow-up intervention strategies (Table 6).[40] Reminder systems, such as cell phone calls, alerts, and text messaging, have been found to be particularly effective for adolescents and young adults.[2,38] A pilot randomized trial of persons aged 15 to 24 years who were nonadherent to antiretroviral therapy found that participants randomized to receive daily cell phone calls had improved self-reported adherence and reduced HIV RNA levels compared with controls who did not receive calls. In another randomized trial that enrolled poorly adherent adolescents and young adults living with HIV infection aged 16 to 29 years, participants who received text message reminders were 2.6 times more likely to be at least 90% adherent after 3 months than those who did not receive the reminders.[41,42] For adolescents who continue to struggle with adherence despite multidisciplinary approaches, antiretroviral therapy may need to be temporarily discontinued to avoid inducing antiretroviral drug resistance. In these situations, when an antiretroviral regimen is restarted, it should include medications with high genetic barriers to resistance.
Preexposure Prophylaxis (PrEP)

Preexposure prophylaxis (PrEP) is an important prevention strategy for persons who are at high risk of acquiring HIV, with several landmark clinical trials demonstrating safety and efficacy in preventing HIV acquisition in men who have sex with men (MSM) and in men and women in heterosexual HIV-discordant couples.\[43,44,45,46,47\] Most of these trials included a significant proportion of young adults aged 18-24 years in the patient population enrolled, but very few included few adolescents (age younger than 18 years). On the basis of these study results, the U.S. Public Health Service issued clinical practice guidelines for the use of PrEP in May 2014.\[48,49\] More recently, several smaller studies have confirmed the safety of using PrEP in adolescent populations.\[50,51,52\] In two companion demonstration projects involving adolescents aged 15 to 17 (Adolescent Medicine Trials Network for HIV/AIDS Interventions [ATN] 113) and young adults aged 18 to 22 men who have sex with men in cities across the United States, PrEP was found to be safe and well-tolerated, but adherence to PrEP decreased over time.\[50,51\] In the first 24 weeks of the studies, the participants had a high incidence of sexually transmitted infections (18 per 100 person-years in adolescents, 76.48 per 100 person-years in young adults), thereby indicating a high risk of HIV acquisition in these groups. Additional studies are needed to further evaluate PrEP in adolescent and young adult populations (only MSM have been studied).

Recommendations for Preexposure Prophylaxis in Youth

For young adults aged 18-24 years at risk for HIV infection, guidelines for PrEP are the same as adults at risk for HIV infection.\[48,49\] Because large randomized studies of PrEP did not involve persons under the age of 18, there is no formal guidance regarding use of PrEP in adolescents.\[51\] Nevertheless, based on findings from ATN 113, in May 2018, the United States FDA approved tenofovir DF-emtricitabine for PrEP in adolescents at risk for HIV who weigh at least 35 kilograms (77 pounds). With the potential to use of PrEP in adolescents, infrastructure for coordinated delivery of HIV prevention services for adolescents are needed that include HIV testing programs that link at-risk youth who test HIV negative to PrEP services.\[25,53\] Prescribing PrEP to adolescents can be complicated by parental consent laws that vary by state.\[48,51\] Adolescent PrEP programs should ideally include adherence support strategies, such as more frequent visits (i.e. monthly instead of quarterly) and pill reminder calls.\[50,51\] Implementing PrEP programs for adolescent populations poses several additional challenges, including medical providers in general have greater comfort prescribing PrEP to adults versus adolescents.\[54,55\]
Immunizations

General Principles for Vaccine Administration in Youth with HIV

The Advisory Committee on Immunization Practices (ACIP) publishes separate annual guidelines for the use of vaccines in children and adolescents (birth-18 years) and for adults (age 19 and older), with both guidelines including routine immunization schedules and immunization schedules based on medical and other conditions.[56,57,58] All inactivated vaccines are considered safe to administer to adolescents and young adults with HIV infection, irrespective of immune status. Accordingly, the ACIP recommends that all adolescents with HIV through age 18 years of age should receive most vaccines per standard recommended (or catch-up) schedules, with the following major exceptions:

1. Precaution should be used when administering rotavirus vaccine.
2. The measles-mumps-rubella (MMR) and varicella vaccines are contraindicated if the CD4 percentage is less than 15 or the CD4 count is less than 200 cells/mm$^3$.
3. Modified dosing schedules are required for Haemophilus influenzae type b, pneumococcal conjugate, pneumococcal polysaccharide, meningococcal ACWY, and human papilloma virus (HPV) vaccines.[57,58]

The following summaries provide additional details for some of the immunizations in adolescents and young adults. In addition, the topic of immunizations in adults reviewed in detail in a separate Topic Review in the Basic HIV Primary Care Module: Immunizations in Adults.

Human Papillomavirus (HPV) Vaccine

The ACIP recommends routinely administering a 3-dose series of the 9-valent HPV vaccine (9vHPV) for all males and females with HIV infection who are aged 11 to 26 years; the series may be started as early as 9 years of age (and should be started at age 9 in children with a history of sexual abuse or assault).[58] In healthy adolescents, a 2-dose schedule for HPV vaccine can be used if started prior to age 15. In contrast, all adolescents and young adults with HIV infection should receive the 3-dose vaccine schedule, regardless of what age the HPV vaccine series is started.[57,58,59] Three HPV vaccines are licensed for use in the United States—bivalent (2vHPV), quadrivalent (4vHPV), and 9-valent (9vHPV), but the 9-valent vaccine is now the only HPV vaccine available in the United States.[59]

Influenza

Annual inactive influenza vaccine is recommended for all adolescents and young adults.[56,57] The recombinant influenza vaccine should not be administered to persons younger than 18 years of age. The live attenuated influenza vaccines should not be administered to any person with HIV infection.[56,57]

Meningococcal ACWY Vaccine

For the general pediatric and adolescent population, the quadrivalent conjugate meningococcal vaccination is recommended beginning at age 11 or 12.[57] In contrast, for children with HIV infection, immunization should begin at 2 months of age.[60] For older adolescents and young adults who have not previously received the conjugate quadrivalent meningococcal vaccine, a two-dose initial series should be given 8-12 weeks apart, followed by booster doses every 5 years.[60] A booster dose is also recommended every 5 years for adolescents and young adults who received the conjugate vaccine as a child. If the initial meningococcal series was administered prior to age 7, then the first booster dose should be given 3 years after completing the primary series and then subsequent booster doses given every 5 years.[60] If the child was age 7 or older when the primary series was given, then the first booster dose should be given 5 years after the primary series was completed and then subsequent booster doses should be given every 5 years. Either the MenACWY-D or MenACWY-CRM can be used as the conjugate meningococcal vaccine, but the same product should ideally be used for all doses.[60] The MenACWY-D vaccine should not be given within 4 weeks...
of the conjugate pneumococcal vaccine.

**Meningococcal B Vaccine**

The serogroup B conjugate meningococcal vaccine is considered an optional vaccine for youth 16-23 years old; the ACIP category B recommendation allows for individual clinical decision-making related to administering the meningococcal B vaccine; age 16-18 is the preferred age range to give this vaccine.[61,62] There are no specific recommendations for administration of meningococcal B vaccine for persons with HIV infection. The ACIP recommends administering meningococcal B vaccine to all persons 10 years of age and older who have increased risk of meningococcal B disease (e.g. persistent complement component deficiencies, anatomic or functional asplenia, microbiologists routinely exposed to *N. meningitidis*, and those at risk because of an outbreak).[61,62] There are no specific recommendations for administration of meningococcal B vaccine for persons with HIV infection.[56,57] Two meningococcal B vaccines are available: MenB-FHbp and MenB-4C. For healthy persons, the dosing schedule for MenB-FHbp is a 2-dose series administered at 0 and 6 months or a 3-dose series administered at 0, 1-2, and 6 months); for MenB-4C, all persons receive a 2-dose series administered at 0 and 6 months.[62] In the general population, both of these vaccines have been shown to be safe and to generate strong immunologic responses.[63,64,65] The ACIP does not give preference of one vaccine over the other, but the same vaccine must be used for all doses in the vaccine series. If the MenB-FHbp vaccine is given to persons with HIV, experts recommend giving the 3-dose series; for persons with HIV who receive the MenB-4C vaccine, the 2-dose schedule is recommended.[66] There are no recommendations to give booster doses for the meningococcal B vaccine.

**Pneumococcal Vaccine**

The ACIP recommends that all adolescents and young adults with HIV be given pneumococcal vaccine starting at entry into HIV care, according to the following strategy regarding the 13-valent pneumococcal conjugate (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23):[56,58]

- If neither PCV13 nor PPSV23 has been received previously, administer 1 dose of PCV13 now and 1 dose of PPSV23 at least 8 weeks later. One additional dose of PPSV23 should be given 5 years after the first dose of PPSV23, and then again at age 65.
- If PCV13 has been received previously but PPSV23 has not, administer 1 dose of PPSV23 at least 8 weeks after the most recent dose of PCV13. One additional dose of PPSV23 should be given 5 years after the first dose of PPSV23, and again at age 65.
- If PPSV23 has been received but PCV13 has not, administer 1 dose of PCV13 at least 8 weeks after the most recent dose of PPSV23. One additional dose of PPSV23 should be given 5 years after the first dose of PPSV23, and again at age 65. Note the recommendation to administer PCV13 at least 8 weeks after the most recent dose of PPSV23 is for adolescents aged 18 years and younger with HIV.[58] For adults with HIV, the ACIP recommends waiting at least 1 year after the most recent PPSV23 before giving the PCV13 dose.[67]

**Tetanus and Diphtheria Toxoids and Acellular Pertussis (Tdap) Vaccine**

The CDC and ACIP recommend that adolescents living with HIV, regardless of CD4 count or percentage should receive one dose of the tetanus, diphtheria, acellular pertussis (Tdap) vaccine at age 11 or 12.[58] The Tdap dose at age 11 or 12 should be given regardless of the interval from the last Tdap vaccination.

**Varicella Vaccine**

Because varicella vaccine is a live attenuated vaccine, adolescents and young adults with HIV
infection should not receive this vaccine if their CD4 count is less than 200 cells/mm\(^3\).\[68\] The following summarizes recommendations for administering varicella vaccine to non-immune adolescents and young adults.

- Adolescents and young adults without evidence of varicella immunity should receive two doses of the single antigen varicella vaccine administered subcutaneously, 4–8 weeks apart. If more than 8 weeks elapses after the first vaccine dose, the second dose should be administered without restarting the schedule.\[69\]
- Adolescents and young adults who received only one dose of varicella vaccine as a child (and do not have history of chickenpox), should receive a one-dose catch-up varicella vaccine.\[69\]
- All adolescents and young adults who receive varicella vaccine should be instructed to return promptly for evaluation if they develop a varicella-like rash following receipt of the vaccine.\[68\]
Adolescent Sexuality, Gender, and Reproductive Health

Sexual Risk Behavior

Adolescence is often a period of heightened sexual and drug activity, which has significant implications for adolescents and young adults living with HIV infection and for those at risk of acquiring HIV.[70] In general, adolescents and young adults living with HIV have different rates of sexual activity based on whether they acquired HIV perinatally or behaviorally. In one sample of youth aged 10 to 16 years who acquired HIV perinatally, 16% reported being sexually active, but 65% of those who were sexually active reported condomless sex.[71] In a separate study, among adolescents who acquired HIV perinatally, 28% reported sexual intercourse, with 62% of the sexually active adolescents reporting condomless intercourse and only 33% disclosing their HIV status to their first sex partner.[31] The Longitudinal Epidemiologic Study to Gain Insight into HIV/AIDS in Children and Youth (LEGACY) evaluated 752 adolescents and young adults (aged 13 to 24 years) living with HIV at 22 clinics in the United States and found that a significantly higher percentage of youth who became infected as adolescents or young adults were sexually active when compared with youth who acquired HIV perinatally (89.5% versus 34.1%).[70] In addition, among the sexually active youth enrolled in the study, those who acquired HIV as an adolescent or young adult had a higher rate of sexually transmitted diseases than those with perinatal HIV acquisition (32.1% versus 10.3%).[70] In another cross-sectional study involving 2,198 youth with HIV aged 12 to 26 years, those infected with HIV as adolescents and young adults were found to have a higher number of recent sex partners and more episodes of condomless sex with serodiscordant partners compared with those with perinatally acquired HIV infection (Figure 14).[72]

Screening for Sexually Transmitted Diseases

All adolescents and young adults living with HIV should undergo screening for sexually transmitted diseases according to 2015 Sexually Transmitted Diseases Treatment Guidelines.[73] These guidelines recommended sexually transmitted diseases screening for all sexually active persons with HIV at the initial HIV care visit and at least annually thereafter.[73] Specific screening should be performed at genital and extragenital sites for curable sexually transmitted diseases (e.g. syphilis, gonorrhea, and chlamydia).[73]

Contraceptive Management

Sexually active adolescent and young adult women with HIV infection should have access to the same array of contraceptive options as older women living with HIV, including hormonal contraception (e.g. pill, ring, injection, or implant) and intrauterine devices (IUDs). Significant drug interactions can occur between hormonal contraceptives and certain antiretroviral medications; these interactions are detailed in the Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV in the table on Drug Interactions Between Antiretroviral Agents and Hormonal Contraceptives.[74] The CDC has published the U.S. Medical Eligibility Criteria for Contraceptive Use (US MEC), which provides specific guidance regarding hormonal contraceptive use for women at high risk for acquiring HIV infection).[75] These guidelines take into consideration the available data related to HIV acquisition or transmission associated with hormonal contraception use and the benefits of preventing unintended pregnancy. A full discussion of contraceptive management for HIV in persons living with HIV is available in a separate Topic Review: Women and HIV.

Sexual Minority Adolescents and Young Adults Infected With HIV

Gay, bisexual, and other young men who have sex with men (YMSM), particularly those who are black, bear a disproportionate burden of youth living with HIV in the United States and require additional psychosocial and healthcare interventions.[2,76] Moreover, young sexual minority (those
who do not identify as heterosexual) males are less likely than young women and heterosexual males to be receiving antiretroviral therapy.[72,76] Information on gender identity is not consistently collected or documented in current HIV surveillance systems, but studies have reported a high HIV prevalence among transgender persons (approximately 20-30%), particularly among transgender women.[77,78,79] Sexual minority adolescents and young adults with HIV infection face barriers to care, such as discrimination, low education level, low perceived risk, and family and social isolation, as well as structural barriers, such as decreased access to identity-affirming healthcare clinics and providers.[80]
Special Considerations for Youth with Perinatal HIV Infection

Informing Children and Adolescents of Their HIV Status

For children who have acquired HIV perinatally, the timing of informing them of their HIV infection status is a highly sensitive and complicated issue. Studies of youth who acquire HIV perinatally found 10 years of age was the typical time for informing a youth of their HIV status, which is older than for many other chronic conditions.[70] The LEGACY study that included 571 youth with perinatally-acquired HIV found that 32% of those aged 13 years and older were unaware of their HIV status and 25% of those unaware of HIV status were sexually active.[70] Lack of knowledge of HIV status as a young person who is entering adolescence is problematic and has obvious implications for HIV transmission.[70,81] The American Academy of Pediatrics strongly encourages disclosure of HIV infection to school-aged children and states that adolescents should know their HIV status and be informed about the consequences of their health behaviors, including sexual activity.[82]

MENTAL HEALTH

Adolescents and young adults who were perinatally infected with HIV have higher rates of mental health disorders compared with uninfected peers, as shown in one study that found a 12-month psychiatric disorder prevalence of nearly 70% among adolescents and young adults living with HIV (or with a history of exposure to HIV).[83] An extensive literature review further confirmed the high prevalence rates of psychiatric disorders in youth living with HIV.[84] According to a review of 8 small studies involving youth living with HIV (who acquired HIV perinatally), the most common mental health disorders were attention deficit hyperactivity disorder (28.6%), anxiety (24.3%), and depression (25%).[85] Youth with perinatally-acquired HIV may also have high rates of behavioral, developmental, and neurocognitive disorders.[86,87] Interestingly, studies evaluating adolescents who were HIV-exposed in utero but not infected with HIV have found high rates of mental health disorders similar to rates in the population of adolescents living with HIV, suggesting families affected by HIV have characteristics, such as substance use, disrupted attachments due to parental illness and death, and poverty, that may play a larger role than HIV in the risk of developing mental health disorders.[81,88]
Transiting to Adult Care

Transitioning from Adolescent to Adult Care

Adolescents and young adults with chronic diseases, including HIV, may face a difficult time in transitioning from adolescent to adult healthcare settings. The transition may be complicated by several different factors, including the presence of coexisting developmental or psychosocial delays, attachment to pediatric/adolescent providers, difficulty trusting a new provider, adjustment to an adult care setting that typically has less psychosocial support and allows less time per encounter, insurance and financial issues, and a lack of communication between pediatric and adult providers.\[2, 10, 18, 89, 90, 91\] Medical providers and institutions transition youth to adult clinics at different ages (some at age 18, some at age 21, and some at age 24 or 25), so the maturity of the transitioning adolescent/young adult often varies in different health care settings. Adolescents with perinatal HIV infection may struggle with additional burdens, such as loss of a parent to HIV infection and stigma relating to their condition.\[89, 90\] Because of these many factors, there is often a high rate of attrition, and even an increase in mortality among adolescents with HIV infection as they transition from the pediatric/adolescent multidisciplinary care setting to the adult medical care setting.\[90, 92\]

Models of Transition to Adult Care

The concept of health care transition, which has been defined as the purposeful planned movement of children with special health needs from child-centered to adult-centered care, is a relatively new frontier for HIV medicine, since children living with HIV did not typically survive to adulthood prior to the availability of effective antiretroviral therapy.\[89, 91, 93\] Researchers have found that an organized, deliberate, developmentally appropriate, and compassionate process of medical care transition can improve outcomes as adolescents and young adults enter adult care settings.\[10, 94\] Adolescents and young adults should be included in the conversations around transition, as there are clear discrepancies between what adolescents and young adults need and expect from their medical home, and what they experience.\[Table 7\].\[13\] Various facilitators to a successful transition have been identified, such as developing a relationship with the new adult provider prior to the actual transition, educating adult HIV care teams about transition, developing an individualized transition plan, and providing a formal written transition document.\[2, 10, 89, 90, 94\] There are, however, no evidenced-based guidelines or models to inform the type of transitional care that should be provided to adolescents and young adults living with HIV.
Summary Points

- The HIV epidemic among adolescents and young adults encompasses two very different populations: those who were infected through perinatal transmission (vertical transmission) and those who acquired HIV through risk behaviors, including sex or injection drug use (horizontal transmission).
- Adolescents and young adults in the United States comprised 6% of persons living with diagnosed HIV infection at year-end 2014; a disproportionate number of these youth living with HIV are African American or Hispanic/Latino.
- In 2015, adolescents and young adults accounted for 23% of persons newly diagnosed with HIV and a disproportionate number of these new infections in youth were African American or Hispanic/Latino.
- Male-to-male sex represents the highest risk category for both adolescents and young adults.
- HIV testing rates are low among adolescents and young adults, and less than half of persons infected with HIV who are 13 to 24 years of age are aware of their HIV status.
- The American Academy of Pediatrics strongly encourages disclosure of HIV infection to school-aged children and states that adolescents should know their HIV status and be informed about the consequences of their health behaviors, including sexual activity.
- All adolescents and young adults living with HIV should receive antiretroviral therapy, both for their own health benefit and to reduce the risk of HIV transmission to others.
- For adolescents, antiretroviral therapy selection and dosing is based on sexual maturity rating rather than on age.
- Adolescents and young adults living with HIV may struggle with adherence and often have lower rates of viral suppression when compared with older adults living with HIV.
- Most adolescents and young adults living with HIV are sexually active, with higher rates of sexual activity reported among those behaviorally infected compared with those perinatally infected.
- Researchers have found that an organized, deliberate, culturally competent, developmentally appropriate, and compassionate process of transition can improve health outcomes as adolescents and young adults enter adult care settings.

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[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

[PubMed Abstract] -

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[PubMed Abstract] -

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[PubMed Abstract] -

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[PubMed Abstract] -

[PubMed Abstract] -

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Figures

Figure 1 HIV Cascade of Care for Youth Aged 13 to 29 Years, 2010

Figure 2 HIV Continuum of Care for Youth Aged 13 to 24 Years, 2014

Figure 3 Components of Youth Medical Home Model

Source: Tebb KP, Pica G, Peake K, Diaz A, Brindis CD. Adolescent and Health Professional Perspectives on the Medical Home: Improving Health Care Access and Utilization Under the Affordable Care Act: Philip R. Lee Institute for Health Policy Studies and Division of Adolescent and Young Adult Medicine, Department of Pediatrics, University of California, San Francisco; July 2016.
Figure 4 Persons Living with Diagnosed HIV Infection in United States, by Age, Year End 2015

This graph shows that among persons living in the United States with diagnosed HIV at year end 2015, 3.7% (36,492 of 973,846) were 13-24 years of age.

This graph shows that among persons newly diagnosed with HIV infection in the United States in 2016, 21.2% (8,451 of 39,782) were 13-24 years of age at the time of diagnosis.

Figure 6 New Diagnoses of HIV Infection in United States Adolescents and Young Adults, 2011-2016

As shown, the number of new HIV diagnoses for persons 13-19 (adolescent) and 20-24 years of age was relatively stable from 2001 through 2016. This graphic also shows the annual number of new HIV diagnoses in young adults far outnumbers those in adolescents.

**Figure 7 Adolescents and Young Adults, Living with Diagnosed HIV Infection in United States, by Race/Ethnicity, Year End, 2015**

This graphic shows the estimated number of adolescents and young adults living with diagnosed HIV infection in the United States, based on race/ethnicity. Note the number of African-American youth with HIV outnumbers whites by more than 4-fold.

Figure 8 Rate of Adolescents and Young Adults Living with Diagnosed HIV by Race/Ethnicity, United States, Year End 2015

Among persons ages 13-14, 15-19, and 20-24, black/African Americans have the highest rates of HIV infection.


<table>
<thead>
<tr>
<th>Racial/Ethnic Group</th>
<th>Living with Diagnosed HIV (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age 13-14</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>7.1</td>
</tr>
<tr>
<td>Asian</td>
<td>3.0</td>
</tr>
<tr>
<td>Black/African American</td>
<td>40.5</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>5.5</td>
</tr>
<tr>
<td>Native Hawaiian/Other Pacific Islander</td>
<td>6.3</td>
</tr>
<tr>
<td>White</td>
<td>2.0</td>
</tr>
<tr>
<td>Person of Multiple Races</td>
<td>15.0</td>
</tr>
<tr>
<td>Average Rate</td>
<td>8.7</td>
</tr>
</tbody>
</table>
Figure 9 New HIV Diagnoses in Adolescents and Young Adults: by Race/Ethnicity, United States, 2016

This graphic shows the estimated number of adolescents and young adults living with newly diagnosed HIV infection in the United States in 2016, based on race/ethnicity. Note the number of African-American youth newly diagnosed with HIV outnumbers whites by more than 3-fold.

**Figure 10 Persons Living with Diagnosed HIV, Aged 13 to 24 Years, by Region of Residence, 2015**

This graphic shows that among adolescents and young adults living with HIV in the United States, more reside in the South than any other region.

Figure 11 HIV Testing Prevalence Among High School Students by Year and Sexual Activity

This graphic shows the percentage of high school students ever tested for HIV during the years 2005-2013 based on sexual activity. The data was obtained from the National Youth Risk Behavior Survey (YRBS) and Behavioral Risk Factor Surveillance System (BRFSS).

Figure 12 Proportion of Persons Living with HIV Unaware of Their HIV Status: by Age Group, United States, 2014

This graph shows that among persons living with HIV, those aged 13-24 years have the highest percentage with undiagnosed HIV and are thus unaware of their HIV status.

**Figure 13 Youth Risk Behavior Survey (YRBS) HIV Test Settings for Young Adults Ever Tested for HIV**

This graphic shows the test setting for young adults ever tested for HIV. The data was obtained from the National Youth Risk Behavior Survey (YRBS) and Behavioral Risk Factor Surveillance System (BRFSS). The setting where they were last tested was used if more than one HIV test had been obtained. Fewer than 5% were tested at an HIV testing site.

Figure 14 Sexual Risk Behavior Among Youth Living with HIV Aged 12-26 Adolescent Medicine Trial Network (ATN) Sites, 2009-2012

The ATN data was collected between 2009–2012 from 20 cross-sectional surveys completed by 649 youth with perinatal HIV infection and 1,547 youth with behavioral HIV infection.

Table 1.
Sexual Maturity Rating (Tanner Staging) in Adolescents

<table>
<thead>
<tr>
<th>Stage</th>
<th>Female</th>
<th></th>
<th></th>
<th></th>
<th>Male</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age Range (years)</td>
<td>Breast Growth</td>
<td>Pubic Hair Changes</td>
<td>Other changes</td>
<td>Age Range (years)</td>
<td>Testes growth</td>
<td>Penis growth</td>
<td>Pubic hair growth</td>
</tr>
<tr>
<td>I</td>
<td>0-15</td>
<td>Pre-adolescent</td>
<td>None</td>
<td>Pre-adolescent</td>
<td>0-15</td>
<td>Pre-adolescent testes (≤2.5 cm)</td>
<td>Pre-adolescent</td>
<td>None</td>
</tr>
<tr>
<td>II</td>
<td>8-15</td>
<td>Breast budding (thelarche); areolar hyperplasia with small amount of breast tissue</td>
<td>Long downy pubic hair near the labia, often appearing with breast budding or several weeks or months later</td>
<td>Peak growth velocity often occurs soon after stage II</td>
<td>10-15</td>
<td>Enlargement of testes; pigmentation of scrotal sac</td>
<td>Minimal or no enlargement</td>
<td>Long downy hair, often appearing several months after testicular growth; variable pattern noted with pubarche</td>
</tr>
<tr>
<td>III</td>
<td>10-15</td>
<td>Further enlargement of breast tissue and areola, with no separation of their contours</td>
<td>Increase in amount and pigmentation of hair</td>
<td>Menarche occurs in 2% of girls late in stage III</td>
<td>1½-16.5</td>
<td>Further enlargement</td>
<td>Significant enlargement, especially in diameter</td>
<td>Increase in amount; curling</td>
</tr>
<tr>
<td>IV</td>
<td>10-17</td>
<td>Separation of contours; areola and nipple form secondary mound above breasts tissue</td>
<td>Adult in type but not in distribution</td>
<td>Menarche occurs in most girls in stage IV, 1-3 years after thelarche</td>
<td>Variable: 12-17</td>
<td>Further enlargement</td>
<td>Further enlargement, especially in diameter</td>
<td>Adult in type but not in distribution</td>
</tr>
<tr>
<td>V</td>
<td>12.5-18</td>
<td>Large breast with</td>
<td>Adult in distribution</td>
<td>Menarche occurs in 10% of</td>
<td>13-18</td>
<td>Adult in size</td>
<td>Adult in size</td>
<td>Adult in distribution (medial)</td>
</tr>
<tr>
<td>Stage</td>
<td>Age Range (years)</td>
<td>Female</td>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Breast Growth</td>
<td>Pubic Hair Changes</td>
<td>Other changes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>single contour</td>
<td>girls in stage V.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Penis growth</td>
<td>Pubic hair growth</td>
<td>Other changes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Testes growth</td>
<td>aspects of thighs; linea alba</td>
<td>and muscles continue to increase in size for several months to years; 20% of boys reach peak growth velocity during this period</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source:
Table 2. **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV**

### Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use (listed in alphabetical order).

<table>
<thead>
<tr>
<th>Integrase Strand Transfer Inhibitor + 2 Nucleoside Reverse Transcriptase Inhibitors:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Note:</strong> For individuals of childbearing potential, see the table Considerations Before Initiating Dolutegravir and Other Integrate Strand Transfer Inhibitors as Initial Therapy before prescribing one of these regimens.</td>
</tr>
</tbody>
</table>

- Bictegravir-tenofovir alafenamide-emtricitabine (AI)
- Dolutegravir-abacavir-lamivudine<sup>a</sup> (AI)—if HLA-B<sup>*</sup>5701 negative
- Dolutegravir plus tenofovir alafenamide<sup>b</sup>-emtricitabine (AI)
- Dolutegravir plus tenofovir DF<sup>b</sup>-emtricitabine<sup>a</sup> (AI)
- Raltegravic<sup>c</sup> plus tenofovir DF<sup>b</sup>-emtricitabine<sup>a</sup> (BI)
- Raltegravic<sup>c</sup> plus tenofovir alafenamide<sup>b</sup>-emtricitabine (BI)

<sup>a</sup>Lamivudine may substitute for emtricitabine or vice versa, if a non-fixed dose NRTI combination is desired.

<sup>b</sup>Tenofovir alafenamide and tenofovir DF are two forms of tenofovir approved by the FDA. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, while tenofovir DF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

<sup>c</sup>Raltegravir can be given as 400 mg twice daily or 1200 mg (two 600-mg tablets) once daily.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Source:
Table 3. **Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV**

**Recommended Initial Regimens in Certain Clinical Situations**

These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred.

**Integrase Strand Transfer Inhibitors + 2 Nucleoside Reverse Transcriptase Inhibitors:**

Note: for individuals of childbearing potential, see the table Considerations Before Initiating Dolutegravir and Other Integrase Strand Transfer Inhibitors as Initial Therapy before prescribing one of these regimens.

<table>
<thead>
<tr>
<th>Regimen Description</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elvitegravir-cobicistat-tenofovir alafenamide(^b)-emtricitabine (BI)</td>
<td></td>
</tr>
<tr>
<td>Elvitegravir-cobicistat-tenofovir DF(^b)-emtricitabine (BI)</td>
<td></td>
</tr>
<tr>
<td>Raltegravir(^c) plus abacavir-lamivudine(^a) (CII)—if HLA-B*5701 negative and HIV RNA (&lt;100,000) copies/mL</td>
<td></td>
</tr>
</tbody>
</table>

**Boosted Protease Inhibitor plus 2 Nucleoside Reverse Transcriptase Inhibitors:**\(^{a, b}\)

(in general, boosted Darunavir is preferred over boosted Atazanavir):

<table>
<thead>
<tr>
<th>Regimen Description</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darunavir plus ritonavir plus tenofovir alafenamide(^b)-emtricitabine(^a) (AI)</td>
<td></td>
</tr>
<tr>
<td>Darunavir plus ritonavir plus tenofovir DF(^b)-emtricitabine(^a) (AI)</td>
<td></td>
</tr>
<tr>
<td>Darunavir-cobicistat plus tenofovir alafenamide(^a)-emtricitabine(^a) (AI)</td>
<td></td>
</tr>
<tr>
<td>Darunavir-cobicistat plus tenofovir DF(^b)-emtricitabine(^a)(AI)</td>
<td></td>
</tr>
<tr>
<td>Atazanavir plus ritonavir plus tenofovir alafenamide(^b)-emtricitabine(^a) (BI)</td>
<td></td>
</tr>
<tr>
<td>Atazanavir plus ritonavir plus tenofovir DF(^b)-emtricitabine(^a) (BI)</td>
<td></td>
</tr>
<tr>
<td>Atazanavir-cobicistat plus tenofovir alafenamide(^b)-emtricitabine(^a) (BI)</td>
<td></td>
</tr>
<tr>
<td>Atazanavir-cobicistat plus tenofovir DF(^b)-emtricitabine(^a) (BI)</td>
<td></td>
</tr>
<tr>
<td>Darunavir plus ritonavir plus abacavir-lamivudine(^a) (BII)—if HLA-B*5701 negative</td>
<td></td>
</tr>
<tr>
<td>Darunavir-cobicistat plus abacavir-lamivudine(^a) (BII)—if HLA-B*5701 negative</td>
<td></td>
</tr>
</tbody>
</table>

**Non-Nucleoside Reverse Transcriptase Inhibitor + 2 Nucleoside Reverse Transcriptase Inhibitors:**

<table>
<thead>
<tr>
<th>Regimen Description</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doravirine-tenofovir DF(^b)-lamivudine (BI)</td>
<td></td>
</tr>
<tr>
<td>Doravirine plus tenofovir alafenamide-emtricitabine (BIII)</td>
<td></td>
</tr>
<tr>
<td>Efavirenz (600 mg) plus tenofovir alafenamide(^b)-emtricitabine(^a) (BII)</td>
<td></td>
</tr>
<tr>
<td>Efavirenz (600 mg)-tenofovir DF(^b)-emtricitabine(^a) (BI)</td>
<td></td>
</tr>
<tr>
<td>Efavirenz (600 mg)-tenofovir DF-lamivudine (BI)</td>
<td></td>
</tr>
<tr>
<td>Rilpivirine-tenofovir DF(^b)-emtricitabine(^a) (BI)—if HIV RNA (&lt;100,000) copies/mL and CD4 count (&gt;200) cells/mm(^3)</td>
<td></td>
</tr>
<tr>
<td>Rilpivirine plus tenofovir alafenamide(^b)-emtricitabine(^a) (BI)—if HIV RNA (&lt;100,000) copies/mL and CD4 count (&gt;200) cells/mm(^3)</td>
<td></td>
</tr>
</tbody>
</table>

**Regimens to Consider when Abacavir, Tenofovir alafenamide, and Tenofovir DF Cannot be Used or Are Not Optimal:**

<table>
<thead>
<tr>
<th>Regimen Description</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolutegravir plus lamivudine (BI)</td>
<td></td>
</tr>
<tr>
<td>Darunavir plus ritonavir plus raltegravir (BID) (CI)—if HIV RNA (&lt;100,000) copies/mL and CD4 (&gt;200) cells/mm(^3)</td>
<td></td>
</tr>
<tr>
<td>Darunavir plus ritonavir once daily plus lamivudine(^a) (BID) (CI)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Lamivudine may substitute for emtricitabine or vice versa, if a non-fixed dose NRTI combination is desired.

\(^b\)Tenofovir alafenamide and tenofovir DF are two forms of tenofovir approved by the FDA. Tenofovir alafenamide has fewer bone and kidney toxicities than tenofovir DF, while tenofovir DF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing...
These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred.

<table>
<thead>
<tr>
<th>between these drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>( ^{a} )Raltegravir can be given as 400 mg BID or 1200 mg (two 600-mg tablets) once daily.</td>
</tr>
<tr>
<td>( ^{b} )Several other NRTI-limiting treatment strategies are under investigation.</td>
</tr>
<tr>
<td>( ^{c} )Lopinavir-ritonavir plus lamivudine is the only boosted PI plus lamivudine regimen with published 48-week data in a randomized controlled trial in ART-naive patients. Limitations of lopinavir-ritonavir plus lamivudine include twice-daily dosing, high pill burden, and greater rates of gastrointestinal side effects than other PIs.</td>
</tr>
</tbody>
</table>

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

Source:

<table>
<thead>
<tr>
<th>Barriers Reported by Participants</th>
<th>Perinatal HIV Infection, % (n = 217)</th>
<th>Youth HIV Infection, % (n = 236)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forgot</td>
<td>75.1</td>
<td>72.9</td>
</tr>
<tr>
<td>Didn’t feel like taking it, needed a break&lt;sup&gt;a&lt;/sup&gt;</td>
<td>39.2</td>
<td>22.0</td>
</tr>
<tr>
<td>Taking it reminds me of HIV, want to forget&lt;sup&gt;a&lt;/sup&gt;</td>
<td>35.5</td>
<td>21.6</td>
</tr>
<tr>
<td>Made me sick to my stomach/tasted bad&lt;sup&gt;a&lt;/sup&gt;</td>
<td>27.6</td>
<td>14.4</td>
</tr>
<tr>
<td>Ran out of prescription</td>
<td>17.5</td>
<td>21.2</td>
</tr>
<tr>
<td>Worried someone would find out about HIV</td>
<td>16.1</td>
<td>19.9</td>
</tr>
<tr>
<td>Got in the way of my daily schedule</td>
<td>17.5</td>
<td>14.4</td>
</tr>
<tr>
<td>Family and/or friends don’t help me remember</td>
<td>17.5</td>
<td>12.3</td>
</tr>
<tr>
<td>Got another illness, wasn’t feeling well</td>
<td>14.7</td>
<td>10.6</td>
</tr>
<tr>
<td>Change in living situation, moved</td>
<td>8.8</td>
<td>12.7</td>
</tr>
<tr>
<td>Can’t get pill at drug store</td>
<td>9.2</td>
<td>12.7</td>
</tr>
<tr>
<td>Get sick even when I take the pills&lt;sup&gt;a&lt;/sup&gt;</td>
<td>14.7</td>
<td>6.4</td>
</tr>
<tr>
<td>Don’t understand why have to take the pills</td>
<td>11.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Nowhere to keep pills at school or work&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Didn’t think I need the pills anymore&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12.0</td>
<td>4.2</td>
</tr>
<tr>
<td>Did not have health insurance</td>
<td>6.0</td>
<td>6.8</td>
</tr>
<tr>
<td>Got a headache, other physical symptom</td>
<td>6.0</td>
<td>6.8</td>
</tr>
<tr>
<td>Family or friends say I shouldn’t take them</td>
<td>1.4</td>
<td>2.1</td>
</tr>
<tr>
<td>Other</td>
<td>22.6</td>
<td>24.2</td>
</tr>
</tbody>
</table>

<sup>a</sup>Percentage of participants endorsing significantly different by route of infection, p ≤.01
<sup>b</sup>Percentage of participants endorsing significantly different by route of infection, p ≤.05

Acknowledgment: This table has been reprinted with permission from Springer Nature: AIDS and Behavior.
Source:

### Evidence-Based Approaches for Monitoring Medication Adherence

<table>
<thead>
<tr>
<th>Routine Assessment of Medication Adherence in Clinical Care</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitor viral load.</td>
<td>Viral load monitoring should be done more frequently after initiating or changing medications</td>
</tr>
<tr>
<td>Assess quantitative self-report of missed doses.</td>
<td>Ask patient and/or caregiver about the number of missed doses over defined period (1, 3, or 7 days).</td>
</tr>
<tr>
<td>Elicit description of medication regimen.</td>
<td>Ask patient and/or caregiver about the name/appearance, number, frequency of medications.</td>
</tr>
<tr>
<td>Assess barriers to medication administration.</td>
<td>Engage the patient and caregiver in dialogue around facilitators and challenges to adherence.</td>
</tr>
<tr>
<td>Monitor pharmacy refills.</td>
<td>Approaches include pharmacy-based or clinic-based assessment of on-time medication refills.</td>
</tr>
<tr>
<td>Conduct announced and unannounced pill counts.</td>
<td>Approaches include asking patients to bring medications to clinic, home visits, or referral to community health nursing.</td>
</tr>
</tbody>
</table>

### Targeted Approaches to Monitor Adherence in Special Circumstances

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implement directly observed therapy.</td>
</tr>
<tr>
<td>Measure plasma drug concentration.</td>
</tr>
</tbody>
</table>

### Approaches to Monitor Medication Adherence in Research Settings

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure drug concentrations in hair.</td>
</tr>
<tr>
<td>Use mobile phone-based technologies.</td>
</tr>
</tbody>
</table>

Source:

- Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV. Guidelines for the use of antiretroviral agents in pediatric HIV infection. Adherence to antiretroviral therapy in children and adolescents living with HIV. May 22, 2018. [AIDSinfo]
<table>
<thead>
<tr>
<th>Strategies for Improving Adherence to Antiretroviral Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial Intervention Strategies</strong></td>
</tr>
<tr>
<td>• Establish trust and identify mutually acceptable goals for</td>
</tr>
<tr>
<td>care.</td>
</tr>
<tr>
<td>• Obtain explicit agreement on the need for treatment and</td>
</tr>
<tr>
<td>adherence.</td>
</tr>
<tr>
<td>• Identify depression, low self-esteem, substance abuse, or</td>
</tr>
<tr>
<td>other mental health issues in the child/adolescent and/or</td>
</tr>
<tr>
<td>caregiver that may decrease adherence. Evaluate and initiate</td>
</tr>
<tr>
<td>treatment for mental health issues before starting antiretroviral drugs, if possible.</td>
</tr>
<tr>
<td>• Identify family, friends, health team members, and others who</td>
</tr>
<tr>
<td>can support adherence.</td>
</tr>
<tr>
<td>• Educate patient and family about the critical role of</td>
</tr>
<tr>
<td>adherence in therapy outcome including the relationship</td>
</tr>
<tr>
<td>between partial adherence and resistance and resistance and</td>
</tr>
<tr>
<td>potential impact on future drug regimen choices. Develop a</td>
</tr>
<tr>
<td>treatment plan that the patient and family understand and to</td>
</tr>
<tr>
<td>which they feel committed.</td>
</tr>
<tr>
<td>• Work with the patient and family to make specific plans for</td>
</tr>
<tr>
<td>taking medications as prescribed and supporting adherence.</td>
</tr>
<tr>
<td>Assist them to arrange for administration in day care, school,</td>
</tr>
<tr>
<td>and other settings, when needed.</td>
</tr>
<tr>
<td>Consider home delivery of medications.</td>
</tr>
<tr>
<td>• Establish readiness to take medication through practice</td>
</tr>
<tr>
<td>sessions or other means.</td>
</tr>
<tr>
<td>• Schedule a home visit to review medications and determine</td>
</tr>
<tr>
<td>how they will be administered in the home setting.</td>
</tr>
<tr>
<td>• Consider a brief period of hospitalization at start of</td>
</tr>
<tr>
<td>therapy in selected</td>
</tr>
</tbody>
</table>
circumstances for patient education and to assess tolerability of medications chosen.

**Medication Strategies**

- Choose the simplest regimen possible, reducing dosing frequency and number of pills.
- When choosing a regimen, consider the daily and weekly routines and variations in patient and family activities.
- Choose the most palatable medicine possible (pharmacists may be able to add syrups or flavoring agents to increase palatability).
- Choose drugs with the fewest adverse effects; provide anticipatory guidance for management of adverse effects.
- Simplify food requirements for medication administration.
- Prescribe drugs carefully to avoid adverse drug-drug interactions.
- Assess pill-swallowing capacity and offer pill-swallowing training and aids (e.g., pill swallowing cup, pill glide). Adjust pill size as needed.

**Follow-Up Intervention Strategies**

- Have more than one member of the multidisciplinary team monitor adherence at each visit and in between visits by telephone, email, text, and social media, as needed.
- Provide ongoing support, encouragement, and understanding of the difficulties associated with maintaining adherence to daily medication regimens.
- Use patient education aids including pictures, calendars, and stickers.
- Encourage use of pill boxes, reminders, alarms, and timers.
- Provide follow-up clinic visits, telephone calls, and text messages to support and assess adherence.
- Provide access to support
groups, peer groups, or one-on-one counseling for caregivers and patients, especially for those with known depression or drug use issues that are known to decrease adherence.

- Provide pharmacist-based adherence support, such as medication education and counseling, blister packs, refill reminders, automatic refills, and home delivery of medications.
- Consider directly observed therapy at home, in the clinic, or in selected circumstances, during a brief inpatient hospitalization.
- Consider gastrostomy tube use in selected circumstances.
- Information on other interventions to consider can be found at [http://www.cdc.gov/hiv/prevention/research/compendium/ma/complete.html](http://www.cdc.gov/hiv/prevention/research/compendium/ma/complete.html)

Source:

Table 7. **Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection**

**Discrepancies Between What Adolescents Want Compared to What Adolescents Experienced**

<table>
<thead>
<tr>
<th>What Adolescents Want</th>
<th>What Adolescents Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Relationship with primary care provider who:</strong></td>
<td></td>
</tr>
</tbody>
</table>
- Knows them and cares about their health;  
- Responds to them as individuals and treats them with respect;  
- Can be accessed on a regular basis; and  
- Can talk to about issues that are important to adolescents. |  
- Lack of an established primary care provider  
- Lack of understanding and respect from their primary care provider  
- Barriers to accessing a primary care provider  
- Insufficient opportunities to talk with primary care provider |
| **Comprehensive care** where physical, mental, vision and dental health care needs are met. |  
- Concerns about privacy and sharing information between providers  
- Limited selection of providers and care |
| **Confidentiality assurances and protections** |  
- Lack of knowledge of existing confidentiality rights and protections for adolescents  
- Barriers to having time alone with primary care providers |

Source:

- Tebb KP, Pica G, Peake K, Diaz A, Brindis CD. Adolescent and Health Professional Perspectives on the Medical Home: Improving Health Care Access and Utilization Under the Affordable Care Act: Philip R. Lee Institute for Health Policy Studies and Division of Adolescent and Young Adult Medicine, Department of Pediatrics, University of California, San Francisco; July 2016. [Health Policy Brief]